

DETAILED ACTION

Re: Browning et al

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/2/2008 has been entered.
2. The amendment filed 5/2/2008 is acknowledged and entered into the record. Accordingly, claims 1-51 are canceled without prejudice or disclaimer, and claims 52-70 are newly added.
3. Claims 52-70 are pending and examined on the merits.

New Rejections

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 52-70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Delgi-Esposti *et al* (previously cited) or Ashkenazi *et al* (previously cited) in view of Renzetti *et al* (WO 97/41895), Etcheverry (WO 96/039488).

- a. The teachings of Delgi-Esposti *et al* and Ashkenazi *et al* have been previously set forth.
- b. Renzetti *et al* teach that the production of TNFR-Ig fusion proteins can be optimized by adjusting among other things the temperature to ensure optimum protein production.
- c. Etcheverry teach that controlling the glycosylation patterns of the recombinant protein may affect among other things the physical properties of a recombinant protein.

It would have been *prima facie* obvious to those of ordinary skill in the art at the time the invention was made to optimize the production condition of the LT β R-fusion proteins as claimed to arrive at a product which would have no more than 30% inactive fusion protein in the composition. Those of skill in the art would have been motivated to generate a higher percentage of "active" protein over inactive protein because the

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"active" form is the working form which can be used for the purpose of treating cancer as taught by Delgi-Esposti *et al.* Although Delgi-Esposti *et al* did not readily recognize that there were two forms of LT β R in their composition, those of skill in the art would recognize that a purified form of the fusion protein was needed for the treatment of cancer. Renzetti *et al* point out that " [f]actors which affect cell specific productivity are well known in the art and include, but are not limited to, factors which affect DNA/RNA copy number, factors which affect RNA, such as factors which stabilize RNA, media nutrients and other supplements, the concentration of transcription enhancers, the osmolality of the culture environment, the temperature and pH of the cell culture, and the like." Those of skill in the art without recognizing that there were multiple forms of LT β R fusion protein would attempt to modify these conditions to achieve the highest production of recombinant protein possible. Moreover, the production of the LT β R fusion protein as provided by Delgi-Esposti *et al* would inherently possess the active and inactive forms of the fusion protein. [T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).

Renzetti *et al*, teach that the production of TNFR-Ig protein was optimized at a temperature range of 30-37 degrees. Therefore, those of skill in the art would

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appreciate that other TNF receptor family members could be produced in CHO cells at a lower than normal temperature and would be motivated to try these temperature for the production of the LT β R fusion protein claimed. The skilled artisan would have expected as reasonable expectation of success in lowering the temperature because by doing so properties such as glycosylation and folding could be enhanced. (see WO 96/39488 Description section which teaches that "[t]he terminal sialic acid component of the glycoprotein oligosacchande side chain affects absorption, serum half life, and clearance from the serum, as well as the physical, chemical and immunogenic properties of the glycoprotein").

Therefore, the skilled artisan would be motivated to optimize the culturing conditions to arrive at a composition which contains a higher ration of "active" protein over "inactive" protein.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER H. YAEN whose telephone number is (571)272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Christopher H Yaen/
Primary Examiner, Art Unit 1643